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Everything You Always Wante...

Everything you always wanted to know about the medical device amendments... and weren't afraid to ask.

Third Edition

U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Devices and
Radiological Health

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August 1990

U.S. Department of Health
and Human Services
Public Health Service
Food and Drug Administration
Center for Devices and
Radiological Health

HHS Publication FDA 90-4173

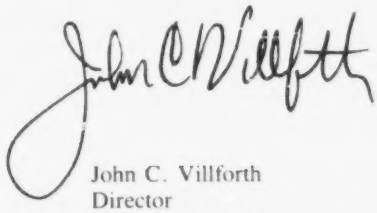
FOREWORD

In October 1982, the Food and Drug Administration established the Center for Devices and Radiological Health (CDRH) by merging the Bureau of Medical Devices and the Bureau of Radiological Health.

The Center develops and implements national programs to protect the public health in the fields of medical devices and radiological health. These programs are intended to assure the safety, effectiveness and proper labeling of medical devices, to control unnecessary human exposure to potentially hazardous ionizing and non-ionizing radiation, and to ensure the safe, efficacious use of such radiation.

The Center publishes the results of its work in scientific journals and in its own technical reports. These reports provide a mechanism for disseminating results of CDRH and contractor projects. They are sold by the Government Printing Office and/or the National Technical Information Service.

We welcome your comments and requests for further information.



John C. Villforth
Director
Center for Devices
and Radiological Health

PREFACE

The medical device industry is young and growing vigorously. The Medical Device Amendments of 1976 (the Amendments) formally initiated regulations to guide this industry, originally by the Bureau of Medical Devices and more recently by the Center for Devices and Radiological Health (CDRH). The purpose of this booklet is to provide the interested reader with an introduction to medical devices and with answers to questions frequently asked about device regulation. Several thousand copies of the 1977 edition of this booklet were distributed to interested individuals and firms.

Most of the regulations implementing the Amendments are now final. Many guidance documents have also been issued to complement these regulations. The answers to a few of the questions in this booklet may change with future policy decisions. Therefore, this booklet should not be viewed as established policy, binding on the Agency. Rather, it is an attempt to clearly portray current views of CDRH officials to provide general guidance for individuals and firms wishing to comply with the Medical Device Amendments of the Federal Food, Drug, and Cosmetic Act.

For additional information, we recommend the following sources:

LAWS ENFORCED BY THE U.S. FOOD AND DRUG ADMINISTRATION. This publication contains the complete Federal Food, Drug, and Cosmetic Act, including Amendments; Public Health Service Act, Biological Products Act; Public Health Service Act, Radiation Control for Health and Safety Act; the Fair Packaging and Labeling Act; and other Laws.

FEDERAL REGISTER. This publication provides all the official notices and proposed and final regulations that are issued by Federal agencies, including FDA. Copies of the *Federal Register* may be obtained by annual subscription.

CODE OF FEDERAL REGULATIONS, TITLE 21—FOOD AND DRUGS [parts 800 to 1299]. This book contains final regulations concerning Medical Devices (parts 800-895), Radiological Health (parts 1000-1050), and certain other regulations administered by the FDA.

These documents may be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402. A copy of the Acts, key *Federal Register* notices, and other printed aids may be obtained by calling the

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Division of Small Manufacturers Assistance, Office of Training and Assistance, CDRH, at 800-638-2041 or 301-443-6597. The mailing address of CDRH and DSMA is: Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

We trust this booklet will be of interest and assistance to you.

H. Neal Dunning

H. Neal Dunning, Director
Division of Small Manufacturers
Assistance
Office of Training and Assistance
Center for Devices
and Radiological Health

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ABSTRACT

Prepared by the Division of Small Manufacturers Assistance, Office of Training and Assistance, CDRH. Project Officers were John F. Stigi, Deputy Director, DSMA, and Arthur C. Kohler, Consumer Safety Officer.

HHS Publication FDA 90-4173 (August 1990), 58 pp. This booklet explains the general regulatory requirements that manufacturers must consider when they manufacture, market, or distribute a medical device. The information is useful for guidance and reference in such regulatory areas as Establishment Registration, Premarket Notification, Premarket Approval, Investigational Device Exemptions, and Good Manufacturing Practices. It is not an official statement of policy binding FDA.

I. Articles Subject to the Medical Device Amendments of 1976

A. Devices [Section 201(h)]

Section 201(h) of the Federal Food, Drug, and Cosmetic Act defines the term "device" as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—

- recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- intended to affect the structure or any function of the body of man or other animals, and

which does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes."

The Medical Device Amendments of 1976 (the Amendments) expanded the definition of "device" to include:

- devices intended for use in the diagnosis of conditions other than disease, such as pregnancy, and
- in vitro diagnostic products, including those previously regulated as drugs.

Examples of devices are: eyeglass lenses and frames, hearing aids, intrauterine devices, surgical devices, surgical instruments, and cardiac pacemakers.

Some devices may be regulated by more than one law. For example, radiation-emitting medical devices must comply with the FD&C Act as amended and the Radiation Control for Health and Safety Act. This concurrent regulation has been simplified by the integration of the Bureau of Medical Devices and the Bureau of Radiological Health into the Center for Devices and Radiological Health. Difficulties may still occur in deciding whether a product is a device, drug, or biological. Advice on whether or not a product is a device may be obtained by calling the Division of Product Surveillance (301-427-1152) or DSMA (800-638-2041).

Q. How do the Amendments apply to a subcontractor who manufactures a finished device for another company?

A. The subcontractor must comply with applicable provisions of the FD&C Act, including registering with the FDA, and complying with the Good Manufacturing Practices regulation.

Q. If a device is assembled from many parts, would the final assembler be regarded as the "manufacturer"?

A. Yes, although it is conceivable that accessories to devices (such as replaceable tubing or optional gauges interchangeable with other devices) may be used in the device as assembled. In this case the assembler and the accessory manufacturer each would be regarded as manufacturers.

Q. Is a sterilizer considered a device?

A. Sterilizers are subject to regulation as devices if they are intended for use in clinical or laboratory settings such as hospitals, clinics, or physicians' offices. Products regulated as devices include biological/physical/chemical sterilization indicators, sterilization pouches, and wraps that are accessories to sterilizers.

B. Diagnostic Products [Section 201(h)]

Under the Amendments, in vitro diagnostic products are considered devices and are, therefore, subject to applicable provisions of the FD&C Act. Unlicensed in vitro diagnostic devices (reagents) intended for use in processing or administration of licensed biologicals are the responsibility of the Center for Drugs and Biologics.

Q. Are general laboratory devices and reagents (e.g., plastic tubing and tube caps) regarded as devices if they are included in an in vitro diagnostic kit?

A. Yes, since these are packaged for sale as device components, parts, or accessories.

Q. How are controls and standards applied to in vitro diagnostic products?

A. Diagnostic products are classified by the appropriate classification panel. This classification determines whether the products are subject to general controls, standards, or premarket approval.

II. Classification of Devices

A. General (Section 513)

The FD&C Act requires FDA to classify all devices intended for human use into one of the three regulatory categories below. These regulatory categories (classes) are assigned according to the extent of control necessary to assure the safety and effectiveness of each device:

Class I, "General Controls": Regulates devices for which controls other than performance standards or premarket approval are sufficient to assure safety and effectiveness. Such controls include regulations that (1) prohibit adulterated or misbranded devices; (2) require domestic device manufacturers and initial distributors to register their establishments and list their devices; (3) grant FDA authority to ban certain devices; (4) provide for notification of risks and of repair, replacement, or refund; (5) restrict the sale, distribution, or use of certain devices; and (6) govern Good Manufacturing Practices, records and reports, and inspections. These minimum requirements apply also to class II and class III devices.

Class II, "Performance Standards": Regulates devices for which general controls alone are insufficient to assure safety and effectiveness and for which existing information is sufficient to establish a performance standard that provides this assurance. Class II devices must comply not only with general controls, but also with an applicable standard developed under section 514 of the FD&C Act. Until performance standards are established by regulation, only general controls apply.

Class III, "Premarket Approval": Regulates devices for which insufficient information exists to assure that general controls and performance standards provide reasonable assurance of safety and effectiveness. Generally, class III devices are those represented to be life sustaining or life supporting, those implanted in the body, or those presenting potential unreasonable risk of illness or injury. New class III devices must have approved Premarket Approval Applications (PMAs). Until premarket approval applications are called for by regulation, pre-amendment class III devices are subject only to general controls.

Panels of experts were established several years ago to provide advice and recommendations to FDA on device classification; this activity continues even though most devices have been classified. After receiving the panel recommendations, FDA determines which class is appropriate and classifies or reclassifies the device by regulation. The proposed classification regulation is then published in the *Federal Register* for public comment before a final order is issued.

Each classification panel section is devoted to a medical specialty and consists of six voting professional members, one nonvoting consumer member, and one nonvoting industry member. The professional members are individuals with training and experience in clinical, scientific,and engineering areas of that medical

specialty. FDA selects its panel member from candidates nominated by professional, consumer, and industry organizations. Qualified candidates are also sought through announcements in the *Federal Register* and in other publications.

In accordance with the Department of Health and Human Services regulations, advisory panel members may serve a 4-year term. A list of these panels appears in Appendix A.

Q. How may a manufacturer obtain current information on the classification status of a device?

A. A manufacturer may contact CDRH to request this information. The written "513(g)" should be sent to the Document Mail Center (HFZ-401), CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850. Informal inquiries about the present classification of any particular device should be directed to DSMA (800-638-2041).

Q. Before a final order on classification, what controls are applied to devices?

A. The general controls provisions of the Amendments apply to all devices currently being marketed. Following final classification, these controls continue to apply.

Devices not "substantially equivalent" to medical devices on the market prior to May 28, 1976, must obtain Premarket Approval. These devices must also comply with the Investigational Device Exemption (IDE) during clinical testing.

Q. How can one seek to have a device reclassified?

A. After a device is finally classified, a manufacturer may elect to petition for reclassification.

Q. What information should a petition for reclassification contain?

A. When final classification is completed, petitions submitted to reclassify a device should include the following information:

- Generic group of devices to which the petition is applicable.
- Action that is requested by the petition, e.g., "It is requested that . . . device(s) be reclassified from class III to class II."
- Completed supplemental data sheet.
- Completed classification questionnaire.
- Full statement of the reasons, with supporting data, why the device should not be classified in its present classification and explanation of how the proposed classification will provide reasonable assurance of safety and effectiveness.

- Summary of new information used to support the petition if that petition is based on new information under sections 513(e), 514(b), or 515(b) of the FD&C Act.

Q. Where should a petition for reclassification be sent?

A. To the Document Mail Center (HFZ-401), CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850. The envelope should be clearly marked with the section of the law under which the petition is being submitted; for example: "513(e) Petition" or other applicable section. The petition and five copies should be submitted on standard size paper.

Q. Does reclassification of a device affect all devices of the same generic type?

A. Yes. Since all devices within a generic group are to be classified into the same class, a petition for reclassification of a specific device is considered a petition to reclassify all devices within that generic group.

However, the manufacturer must make sure that his device falls in the same generic "name" as the device classified.

B. Implantable Devices [Section 513(c)(2)(C)]

If a device intended to be implanted into the human body was marketed before May 28, 1976, enactment date of the Amendments, or if it is substantially equivalent to such a device, it will be classified in class III unless FDA determines that premarket approval is not necessary to provide reasonable assurance of safety and effectiveness. Premarket approval is not required, however, until the device is formally classified by publication of a final regulation in the *Federal Register* (until at least 30 months have elapsed since the final classification date) and until a specific call for PMAs for that device is published in the *Federal Register*. An implantable device not marketed before May 28, 1976, and not substantially equivalent to a pre-amendment device may be marketed only if it has an approved PMA, unless it is reclassified out of class III.

Q. What is FDA's definition of an implanted device?

A. Although FDA has not established a formal definition of a device termed "implant," working definitions have been published in the classification procedures regulation [21 CFR 860.3(d)] and in the IDE regulation [21 CFR 812.3(d)]. The term "implant" means a device (1) that is inserted into a surgically or naturally formed cavity of the human body and (2) that is intended to remain there for a period of 30 days or more. FDA may, at its discretion, determine that devices placed in subjects for shorter periods are also implants.

Q. Could an implantable device for which a 510(k) is submitted be determined by CDRH to be substantially equivalent to a pre-amendment device even if it has significantly unique functional characteristics?

A. Yes, provided those functional changes do not affect the device's safety and effectiveness to the extent that the altered device becomes distinct from those already on the market.

Q. Who is responsible for the performance of a device once it has been implanted?

A. Before *and* after implantations, the manufacturer is responsible for assuring that a device is not adulterated or misbranded and that it is otherwise safe and effective. Also, the health professional is responsible for properly using a device as it was intended. Ultimate responsibility for device failure would depend on the facts specific to each situation and could require a case-by-case analysis.

Q. Will FDA issue regulations governing the literature that accompanies an implantable device?

A. Although specific labeling regulations are established for intrauterine devices and hearing aids, FDA has no specific plans to promulgate labeling requirements exclusively for implantable devices. General labeling regulations, however, do apply. Device labeling includes all written, printed, or graphic matter on or accompanying a device. Any literature accompanying a medical device is subject to the labeling requirements of the FD&C Act. Federal regulations governing labeling of all prescription devices are located in 21 CFR 801.109.

Q. May manufacturers of class III implantable devices that are substantially equivalent to pre-amendment devices collaborate on the clinical data required for a PMA?

A. Yes. Manufacturers may collaborate when they submit PMAs providing clinical data to substantiate the safety and effectiveness of their respective devices.

C. Devices Previously Regulated as Drugs [Section 520(l)]

Certain articles previously regulated as drugs are now devices. These "transitional" devices are automatically classified into class III, but are accorded treatment consistent with their former status as drugs. Thus, articles subject to approved New Drug Applications (NDAs) are regarded as class III devices with approved PMAs; pending NDAs likewise become pending PMAs.

On December 16, 1977, FDA published in the *Federal Register* (Volume 42, pages 63472-63476) a notice containing two lists of devices previously regulated as drugs: those devices for which premarket approval is needed, and those for which premarket approval is not needed. Since that time other products have been regulated as "transitional" devices but no further lists have been published. If you think you have a "transitional" device and it is not in the original publication, call DSMA (800-638-2041) or CDRH's Division of Product Surveillance (301-427-1144).

Q. What is the status of an in vitro diagnostic product that was previously regulated as a drug?

A. The transitional provisions relating to devices previously regulated as drugs, section 520(l), apply to those in vitro diagnostics regulated as new drugs before May 28, 1976, enactment date of the Amendments. This section provides that all such products are automatically classified in class III but are accorded treatment consistent with their former status as drugs. Thus, diagnostic products marketed under approved NDAs before May 28, 1976, are regarded as having approved PMAs.

Q. If a device is part of a drug delivery system that is subject to an NDA, will it be regulated under the Amendments?

A. No. As long as the device is part of the drug container or delivery system or is permanently attached to the drug container, it will be regulated as a drug. Empty delivery systems such as hypodermic syringes and administration sets packaged with drugs, however, are subject to regulation as devices.

III. General Controls

A. Adulteration (Section 501)

In addition to the basic provisions of this section, the Amendments provide that a medical device is considered adulterated if it is a banned device, if it does not comply with a mandatory performance standard or an IDE to which it is subject, or if it is not manufactured in accordance with the device GMP requirements. A class III device is considered adulterated also if it does not comply with the requirements for an approved PMA or a completed Product Development Protocol (PDP) to which it is subject.

B. Misbranding (Section 502)

Provisions for misbranded devices apply to any device that is manufactured in an unregistered establishment or whose advertisements and labeling do not comply with certain requirements for disclosure of product information if the device is restricted under section 520(e). These provisions also govern a device that does not comply (1) with labeling requirements of a mandatory performance standard to which it is subject, (2) with requirements of section 518, notification and other remedies, or (3) section 519, records and reports. The Federal Trade Commission has the primary responsibility for regulating the truth or falsity of medical device advertising other than labeling.

Q. What constitutes labeling?

A. Labeling refers to the label plus any other written, printed, or graphic material that accompanies the device or that is placed on either the device or any of its wrappers or containers. Advertising may be considered labeling, especially if it accompanies the device. Operating and servicing instructions are also regarded as part of the labeling. The labeling must bear adequate directions for use and any warnings needed to ensure the safe use of the device. (See sections 201(k) and (m) and 502(f)(1) and (2) of the FD&C Act.)

Q. Do all devices require directions for use?

A. Yes, unless specifically exempted by regulation. (See 21 CFR 801, subpart D for a list of the conditions for exemption from this requirement.)

Q. Is "truth in labeling" to be enforced for devices?

A. Yes, in accordance with the Fair Packaging and Labeling Act (sections 1451-1461 inclusive, and 21 CFR part 1).

Q. Must labeling of sterilized devices provide information on expiration dates for guaranteed sterility?

A. Only if necessary for safe and effective use of a device as intended by the labeling. FDA does not now require expiration dates for sterile devices. Labeling regulations for in vitro diagnostic devices [21 CFR 809.10 (a) and (b)] require an expiration date or some other means by which the user may be assured of quality at the time of use. This would apply to both sterile and nonsterile in vitro diagnostic devices.

C. Registration and Listing (Section 510)

The FD&C Act requires manufacturers and other specified processors of devices to register their establishments with FDA and to list their devices. Repackers and relabelers, as well as initial distributors of imported devices, must also register with FDA. Registration form FDA-2891 is used.

Manufacturers of raw materials or components used in manufacturing a finished device are exempted from registration if they also market the same material or components to non-device manufacturers and they are not providing the device manufacturer with a "finished" device. Examples of other establishments exempt from registration are:

- Licensed practitioners, including physicians, dentists, and optometrists, who manufacture or alter devices solely for use in their practice.
- Pharmacies and other retail outlets who dispense or sell devices in the normal course of business.
- Persons who manufacture devices solely for use in research, teaching, or analysis and who do not distribute such devices in commerce.
- Warehousers and wholesalers who do not revise devices or their containers.
- Carriers who receive, carry, hold, or deliver devices in their normal conduct of business.
- Persons who dispense devices to the user or who render a service necessary to provide the user with a device or its benefits, i.e., hearing aid dispenser, optician, clinical laboratory, x-ray assembler, dental laboratory, orthotic or prosthetic retailer, and others whose primary responsibility to the user is to dispense or provide a service through the use of a previously manufactured device.

The following are also required to list their devices with FDA (form 2892): domestic firms (except contract manufacturers) with a registration obligation with FDA; manufacturers, relabelers and repackers, and specifications developers and

initial distributors, if either is a specification developer or repacker and/or relabeler of an imported device; and foreign establishments that export devices into the United States. Initial distributors of foreign-manufactured devices comply with device listing by identifying to FDA those foreign firms whose devices they import into this country.

Necessary forms for establishment registration, FDA-2891, and device listing, FDA-2892, may be obtained from DSMA (800-638-2041) or the Device Registration and Listing Branch (HFZ-342), CDRH, FDA, 1390 Piccard Drive Rockville, MD 20850 (301-427-1152).

Q. Is a manufacturer required to register each establishment that is involved in the manufacture of devices?

A. Yes. The manufacturer registers each establishment initially by completing form FDA-2891.

Q. Is registration done only once?

A. No. Each establishment must be re-registered each year. For subsequent annual re-registrations, manufacturers must complete form FDA-2891(a). FDA sends this form to those establishments having valid device registrations for that year. Registration forms are mailed out in separate mailings to spread the effort involved throughout the year. The manufacturer must complete part two of this form, including any necessary changes, and mail it to FDA within six weeks after receipt. Part one of form FDA-2891(a) is retained by the registrant as proof of re-registration.

Q. What information is required on form FDA-2891?

A. Required information includes name, street address, city, state and zip code of the device establishment; all other business trade names used by the establishment; name and address of the owner/operator of each establishment; and name and address of the official correspondent.

Q. What changes must be made in registration information that has already been submitted?

A. Any changes in individual ownership, corporate or partnership structure, official correspondent, or location of the registered device handling activity are to be submitted by letter to the Device Registration and Listing Branch of the CDRH. The letter should include the current registration number and a statement indicating that the information reflects a change in a previous submission. This information must be submitted to FDA within 30 days of such changes.

A record of any changes in the names of officer and directors of

a corporation must be maintained by the establishment's official correspondent, but this information needs to be transmitted to CDRH only on request.

Q. Does the registration number assigned by FDA constitute FDA approval of the establishment or device?

A. No. Registration of an establishment or listing of a device does not in any way denote FDA approval of the establishment or its products.

Q. Are establishments exempted from registration subject to FDA inspection?

A. Yes. As part of the inspection of the ultimate manufacturer of a device, the plant of a component manufacturer, for example, may be inspected.

Q. Must devices be listed by each registered establishment?

A. No. Device listing must be accomplished by owner/operators of the device handling activity. Listing form FDA-2892 contains provisions that allow owner/operators to identify all their establishments involved in the manufacture, repacking or relabeling, specification development, or importation of devices. An instruction booklet for listing devices is provided to registered firms.

Q. Must foreign firms complete the listing form FDA-2892 themselves?

A. Yes, unless the foreign firm that exports devices into the United States authorizes an initial distributor to complete the form FDA-2892 on its behalf. An initial distributor so authorized must be the sole initial distributor of the device(s) listed and must maintain the listing historical file for the device(s). The foreign firm's letter of authorization must be provided to CDRH with the listing form(s) FDA-2892.

Q. What constitutes a listing historical file for a listed device?

A. For a class I device, this file must contain a copy of all labels, package inserts, and a representative sampling of any other labeling. The file for a class II or class III device must include all labeling. Each historical file, regardless of the device's classification, must contain any labeling in which a material change has occurred since the date of initial listing.

Q. Must device labeling be submitted with the listing form FDA-2892?

A. Not necessarily. Device labeling should be submitted with form FDA-2892 only when the owner-operator cannot clearly match the device with one in either of the following booklets provided with the listing packet: "Classification Names for Medical Devices" and "Classification Names for In Vitro Diagnostic Products." FDA may request a device's historical file, however, if it is needed.

D. Premarket Notification [Section 510(k)]

Section 510(k) of the FD&C Act requires those device manufacturers who must register to notify FDA, at least 90 days in advance, of their intent to market a device. This is known as premarket notification. It allows FDA to determine whether the device is equivalent to a device already placed into one of three classification categories. Thus, "new" devices (not in commercial distribution prior to May 28, 1976) that have not been classified can be properly identified.

Specifically, medical device manufacturers are required to submit a premarket notification if they intend to introduce a device into commercial distribution for the first time or to introduce, or reintroduce, a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected. Such change or modification could relate to design, material, chemical composition, energy source, manufacturing process, or intended use.

Premarket notifications should be securely bound, if necessary, and should be submitted in duplicate. They should contain the following information:

- All names of the device, including trade (proprietary) name, common (usual) name, and classification name as defined by the classification panel.
- Registration number of the notifying establishment (if applicable).
- Class of the device and the appropriate classification panel. If the device has not yet been classified, include a statement to that effect.
- Actions taken to comply with performance standards if the device is a class II device and a final FDA standard exists for that device.
- Samples of proposed labels, labeling, and advertisements sufficient to describe the device, its intended uses, and directions for use.
- Statement of how the device is either similar to and/or different from other devices on the market, plus data to support the statement.
- Information describing a significant change or modification, if any occurred, that could affect the device's safety or effectiveness.

Q. How long does FDA have to review a premarket notification?

A. Ninety days—but see the questions and answers following for qualifications.

Q. If FDA receives an incomplete premarket notification and requests additional information to support it, does the 90-day period begin again?

A. If FDA requests additional information, the 90-day "timeclock" officially begins again. The manufacturer must assume that 90 days may be required to review the submission with the added information, even though less time may actually be needed.

Q. Must a firm be registered in order to submit a 510(k)?

A. No. In fact, a new device firm need not register until 30 days after it actually starts manufacturing devices.

Q. If a manufacturer who has submitted premarket notification does not receive an answer from FDA within 90 days, what action should the manufacturer take?

A. CDRH usually answers the manufacturer within 90 days. If a manufacturer receives no answer within 90 days after the submission was received by FDA, the manufacturer may proceed to market the device. It is prudent, however, to determine FDA's response to the premarket notification by having DSMA (800-638-2041) determine whether or not the submission was received and the final disposition.

Q. What happens if a manufacturer and FDA disagree over whether a device is substantially equivalent?

A. Final determination of this issue remains with FDA. A device that is not substantially equivalent is automatically classified into class III and is subject to premarket approval. Under section 513(f) of the FD&C Act, a manufacturer may petition FDA for reclassification of this device into class I or class II. If such a petition is filed, sufficient additional data justifying this petition should be submitted also.

Q. What is the definition of "commercial distribution"?

A. A device is in commercial distribution if it meets the following conditions:

- The device was displayed, advertised, or otherwise offered for sale before May 28, 1976, for a specific intended purpose or purposes, with no limitations (e.g., no limitation to research or investigational use);
- The manufacturer had, before May 28, 1976, accepted or had been prepared to accept, at least one order to purchase the device that resulted, or would have resulted, in a sale of the device in the United States, generally with delivery to oc-

cur immediately or at a promised future date;

- The device was not being offered or accepted for research or investigational use only; and
- The manufacturer of the device can provide adequate documentation establishing (1) through (3) above to the satisfaction of the FDA.

Q. In order to be considered a preamendment device in commercial distribution, must a device have been offered for sale, ordered, or shipped before May 28, 1976?

A. The definition of the term "commercial distribution" applies only to a device that is held or offered for sale. If a device is shipped merely for display as a work-in-process or as an engineering prototype at a scientific exhibit and if it is not held or offered for sale, it is not considered in commercial distribution. If purchase orders are taken for future delivery of the device while it is being displayed, however, it is considered to have been in commercial distribution. (See section I, "Articles Subject to the Amendments" and section V, "Premarket Approval.")

Q. Before May 28, 1976, a device was commercially distributed in two forms for consumer acceptance evaluation. On May 28, one version of the product was temporarily removed from the market for modifications. Since both devices were in commercial distribution before the date of enactment, can both products be marketed without premarket notification?

A. The device that was not removed from the market was clearly in commercial distribution and, thus, does not require premarket notification. The device that was modified could conceivably require premarket notification, depending on the nature of the modifications.

Q. Would research and development samples of a device sold before May 28, 1976, constitute commercial distribution, and would this exempt the device from premarket notification?

A. No. If the samples were sold or shipped exclusively for research and testing purposes, a premarket notification would be required, because the device had not been in commercial distribution.

Q. Does the submission of an IDE application, establishment registration form FDA-2891, or device listing form FDA-2892 fulfill the requirements for premarket notification?

A. No.

Q. Before a final orde. on classification, does a post-amendment class III device that is life sustaining and substantially equivalent to a device marketed before May 28, 1976, require only premarket notification before it can be marketed?

A. Yes. First note that virtually all devices have been classified in final rules. If other applicable general controls for the device have been fulfilled, and no specific regulation calling for a PMA for the device is in effect, the device can be marketed through the premarket notification process.

Q. Can the existence of a premarket notification—a submission under 510(k) of the FD&C Act—be kept confidential?

A. Yes. FDA will keep a premarket notification [510(k)] confidential for 90 days after submission if all of the following conditions are met:

- The submitter has requested confidentiality.
- The product has not been marketed.
- The intent to market the product has not been revealed except to employees, paid consultants, or individuals with contractual arrangements guaranteeing confidentiality.

If you have additional questions about the confidentiality of 510(k)s, call DSMA (800-638-2041).

Q. A sunglasses manufacturer introduces 60 new styles each year. They are all substantially equivalent to pre-amendment devices. Must a premarket notification be submitted for each new style?

A. If the manufacturer has been marketing the sunglasses since before May 28, 1976, and the modifications are only style rather than material changes, the manufacturer need not submit a premarket notification for the modified sunglasses. A premarket notification would be required, however, if the device had not been marketed before enactment of the Amendments or if any of the changes could significantly affect the device's safety or effectiveness. Different styles of a given device may be judiciously grouped so that many "styles" might be covered by a few premarket notification submissions.

Q. Who does *not* need to submit a premarket notification—510(k)?

A. Essentially, premarket notification is not required for pre-amendment devices, devices under the IDE regulation, most transitional devices, and custom devices.

In addition, a number of class I devices have been exempted by regulation from 510(k) requirements. DSMA has a list of these exempted devices (800-638-2041).

An exemption from the 510(k) requirements also applies to an "own-label" distributor and a repackager who places his own name on a device and does not change any other labeling or otherwise affect the device, provided that:

- The device was in commercial distribution before May 28, 1976.
- A premarket notification was filed by another person.

A premarket notification submission is not required to resume commercial distribution of a device that was on the market before May 28, 1976, and was discontinued by the manufacturer.

E. Banned Devices (Section 516)

FDA has the authority to ban by regulation any device intended for human use that presents a substantial deception or an unreasonable and substantial risk of illness or injury. Before initiating such proceedings, however, FDA considers all available information and consults with the appropriate classification panel.

If FDA determines that the deception or risk can be corrected by labeling or by changes in labeling, FDA notifies the manufacturer in writing, pointing out the deception or risk, specifying the labeling changes necessary for correction, and stating the time frame in which the manufacturer must make these changes. If the labeling or changes in labeling are not made within the period specified, FDA may start a proceeding to ban the device. If the device presents an unreasonable, direct, and substantial risk to patients, this proposed regulation would be effective when published in the *Federal Register*, pending an informal regulatory hearing and final action on the proposal.

FDA, as of this writing, has banned one device—synthetic fibers implanted into the human scalp.

Q. May a banned device be used in clinical trials?

A. Yes. An application for an IDE for a banned device, however, must be approved by FDA in writing before the investigation may begin.

F. Notification, Repair, Replacement, or Refund (Section 518)

Section 518(a) of the FD&C Act authorizes FDA to issue an order requiring notification of a risk upon determining that a device presents an unreasonable risk of substantial harm to the public health. The notification is sent to all health professionals prescribing or using the device and to any other persons who should receive notification in order to eliminate the risk. The order requires notifying

the persons exposed to the risk, unless FDA determines that the notification poses a greater danger to health than lack of notification. If the latter is the case, the order requires that the health professionals who prescribe or use the device notify individuals treated with the device of the risk presented and of any action that may be taken to eliminate or reduce the risk. Before the order is issued, FDA consults with those required to give the notice.

"Repair, Replacement, or Refund," section 518(b), authorizes FDA to order manufacturers, importers, or distributors (1) to repair or replace devices presenting unreasonable risk of substantial harm to the public health so that the devices conform with these provisions, or (2) to refund the purchase price, after affording opportunity for an informal hearing.

Requirements include provisions to assure that repair, replacement, or refund actions do not cause unjustifiable economic loss to the manufacturer and practitioners.

Q. What is the difference between an FDA "recall" and a "correction"?

A. "Recall" means a firm's removal or correction of a marketed product that FDA considers in violation of the laws it administers and against which FDA would take legal action. "Correction" means repair, modification, relabeling, destruction, or inspection—including patient monitoring—of a product without its physical removal to another location. A device may be recalled for any of the following reasons:

- Threat or potential threat to consumer (human or animal) safety or well-being.
- Adulteration.
- Gross fraud or deception (misbranding).
- Materially misleading to cause injury or damage.
- Inadequate instructions for use.

Q. What is the difference between a recall and an action taken under the authority of section 518 of the FD&C Act relating to notification and repair, replacement, or refund?

A. The main difference between these actions is that a recall is a voluntary or FDA-requested action taken by the manufacturer. At this time, FDA cannot require a manufacturer either to institute or to report a recall, but FDA can require a manufacturer to take an action under section 518. An action taken under section 518 may subsequently be classified as a recall. Action may be taken under section 518 on a device that is not violative.

Q. When a device is recalled, must the equipment be brought back to the plant?

A. Not necessarily. For example, some recalls involve only a field modification or relabeling.

In some cases, however, it may be necessary to physically return the device, e.g., nonsterile devices labeled as sterile. The manufacturer's action is monitored by FDA and is classified as a recall if the criteria of the definition in 21 CFR part 7 are met.

Q. What testing is required after corrective modifications have been made to a recalled device?

A. Testing must be sufficient to prove that the modification corrected the problem, and resulted in a safe and effective device.

G. Good Manufacturing Practices [Section 520(f)]

The Good Manufacturing Practices (GMP) regulation which enforces section 520(f) became effective December 18, 1978. Its requirements cover the methods, facilities, and controls used in manufacturing, packing, storing, and installing medical devices.

This GMP regulation identifies the essential objectives that must be included in a quality assurance system. A quality assurance program meeting the GMP requirements will ensure that the finished device meets specifications, by reducing manufacturing process variation that can lower quality. Because the regulation covers a broad spectrum of devices, it allows the manufacturer discretion in determining the pertinence or necessity of certain steps and in developing procedures appropriate for the product that satisfy the GMP requirements.

The GMP regulation designates two device categories: "critical" and "noncritical." Critical devices are those intended to be surgically implanted into the human body or to support or sustain human life and whose failure when used according to labeling instructions could reasonably be expected to result in significant injury; all other devices are considered noncritical. General requirements apply to all devices, but critical devices must also meet additional GMP requirements. A current list of critical devices has been published in the *Federal Register.* This list may be updated, however. If you have questions, call the Division of Compliance Programs (301-427-1125) or DSMA (800-638-2041).

Q. What is a GMP exemption or variance?

A. An exemption is an authorization that excuses a manufacturer from complying with all or part of the GMP regulatory requirements. A variance is an authorization to substitute an adequate alternate procedure or practice in lieu of one or more GMP regulatory requirements.

Unless a device is specifically exempted, all medical device manufacturers must comply with the device GMP regulation. Devices may be exempted from the GMP regulation. DSMA maintains a list of these exemptions. Under section 520(f)(2)(A) of the FD&C Act, manufacturers may seek exemption or variance from all or part of the requirements that are, in their

judgment, inappropriate to their manufacturing operations. This provision allows manufacturers, trade organizations, or other interested persons to seek exemption or variance by petitioning FDA.

Q. Do the device GMP regulation requirements apply to foreign manufacturers?

A. Yes. FDA routinely schedules inspections of foreign manufacturers of medical devices.

Q. May a device be exported even though it does not meet the adulteration requirements of the device GMP regulation?

A. A device that does not meet the GMP regulation is adulterated within the meaning of section 501(h) of the FD&C Act, but it may be exported if it complies with section 801(e). (See section XIII, "Import and Export of Devices.")

Some foreign countries may require that the manufacturer meet the device GMP regulation. This is more likely as bilateral inspection agreements are made between the United States and other countries. CDRH is not presently scheduling for GMP inspection those domestic firms who exclusively export, but do not import, medical devices.

Q. Must a manufacturer of components of medical devices comply with the GMP regulation?

A. The manufacturer of "components" of medical devices is, in some cases, subject to the GMP. For example, when a manufacturer fabricates components exclusively for use in a finished medical device which is manufactured in the same facility as the components, the manufacturer has full control of the component manufacturing process. In such cases, component manufacturing is considered part of the production of the finished device and is subject to the applicable requirements of the GMP regulations.

Manufacturers of components who supply only a fraction of their production to finished device manufacturers do not have to comply with the GMP regulations. For example, standard transistors, capacitors, etc., are supplied to the marketplace and are not manufactured exclusively for use in devices. Part 820.1 of the GMP, however, encourages component manufacturers to use the GMP regulations as guidelines where appropriate.

Q. Is a facility repairs a device, is it subject to the device GMP regulation?

A. Not if it simply repairs a device for a user to return it to its original condition. If a firm is in the business of marketing reconditioned devices, it must register and must comply with applicable GMP requirements. Modification causing the device to vary from original specifications is "manufacturing," however, and is subject to the GMP regulation.

Firms that only repair devices must ensure that these devices are still safe and effective. Record-keeping, equipment calibration, and feedback of repair information to the quality assurance program are all important elements of assuring device safety and effectiveness.

Q. What about those who manufacture accessories?

A. An accessory is viewed as any unit which is intended to be attached to or used in conjunction with another finished device, although the accessory may be sold or promoted as an independent unit. Examples include intrauterine device inserters, electrocardiographic printers, electrode paste, blood filters, and hemodialysis tubing sets. Contact the Manufacturing Quality Assurance Branch (HFZ-330), CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850 (301-427-1128) or DSMA (800-638-2041) for information about the GMP.

Q. What is the Device GMP Advisory Committee?

A. This committee is composed of nine members [section 520(f)(3)]. Three members represent Federal, State or local government; two members represent the interests of health care professionals; two members represent the interests of the device manufacturing industry; and two members represent the interests of the general public. Openings appear periodically as terms expire and are announced in the *Federal Register*. Members serve a term of three to four years. Meetings are held as appropriate issues arise.

Q. How are members of the Device GMP Advisory Committee selected?

A. An individual or organization may nominate qualified individuals to serve on this committee, or persons may nominate themselves. The nomination must include a curriculum vitae; a description of current employment background in the medical devices field, if any; and a statement that the nominee is willing to serve and has no apparent conflict of interest. Nominations should be sent to the Executive Secretary of the Device Good Manufacturing Practice Advisory Committee, CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850.

Q. Can a manufacturer be exempt from the entire device GMP regulation?

A. No. Manufacturers must always maintain complaint records and also have an adequate system for complaint investigation and follow-up. (See 21 CFR 820.198.) Manufacturers also must grant authorized FDA employees access to complaint files, device-related injury reports, and failure-analysis records for reviewing and copying. (See 21 CFR 820.180.)

Exemption from the device GMP regulation does not release a manufacturer from the responsibility of assuring that the

finished device has the purity or quality it purports to possess. Within the meaning of section 501(c) of the FD&C Act, a device that does not have the quality or purity it purports to possess is adulterated, and if a device is misbranded or adulterated, it is subject to regulatory action even though it may be exempted from the GMP regulation.

Q. Are devices labeled or otherwise represented as sterile eligible for exemption from the GMP regulation?

A. No. Manufacturers of sterile devices must have a quality assurance program adequate to assure that sterility specifications are met.

Q. Are all implants critical devices?

A. No. A critical device is a device that is intended to be surgically implanted into the body or to support or to sustain life and whose failure to perform when used according to the labeling can be reasonably expected to result in a significant injury to the user. To become a critical device candidate, an implanted device must also meet the second part of the definition, i.e., "...and whose failure to perform...can be reasonably expected to result in a significant injury to the user."

Q. What is a "complaint"? Are repair requests considered complaints?

A. "Complaint" means any written or oral communication concerning dissatisfaction about identity, quality, durability, reliability, safety, effectiveness, or performance of a device as stated in 21 CFR 820.198(a). Routine service requests would normally not be considered complaints, but records should be maintained for detecting any defect trends and determining product reliability. Any reference to dissatisfaction with the device should be considered a complaint.

Q. The device GMP regulation requires that quality audits be conducted by individuals not having direct responsibility for the matters being audited. How may very small firms meet this requirement?

A. Although an independent audit is preferred, FDA places more emphasis on the training and qualifications of auditors than on their independence from the subject area of the audit. If a very small firm—particularly one in which everybody is directly involved in daily production activities—concludes that an independent audit would be unduly burdensome or impractical, the firm may perform its own audit. In such a case, FDA expects the firm to follow a written audit plan, such as a list of the areas to be audited, and record the findings and any

corrections made. Investigators will review a company's audit plans. As a matter of administrative policy, FDA will not seek access to actual internal audit reports during routine GMP inspections. The acceptability of self-audits will be judged on a case-by-case basis.

Q. What are the minimum requirements for a self-audit?

A. In order to meet the requirements of the GMPs, such a self-audit must meet the following minimum requirements:

- The audit must be done by appropriately trained individuals—training may be formal or on-the-job.
- A written audit plan or procedure must be developed, implemented, and available for review and copying by FDA. For a very small operation, the plan might consist of a checklist of areas to be audited and aspects to be checked.
- Audits must be conducted according to a schedule.
- A record must be kept of audit findings and the record must be reviewed by management. When needed, corrective action must be taken.
- Responsibilities must be clearly defined and assigned.

Although a very small firm may not require as much written instructions for its audit as a large firm, it still must document the functions to be audited, the audit findings, and any corrective action taken as a result of the audit.

Several publications may be helpful to the manufacturer interested in more information on GMP requirements. For the most current ones and references to GMP specialists, contact DSMA (800-638-2041).

IV. Performance Standards

Section 514 of the Act gives FDA the authority to issue mandatory standard for class II medical devices. CDRH has published its intention to begin preparation of mandatory standards for the following 11 medical devices:

- Continuous ventilators.
- Vascular graft prostheses of 6mm and greater diameter.
- Cardiac monitors (including cardiotachometers and rate alarms).
- Ventilator tubing.
- Breathing frequency monitors.
- Central nervous system fluid shunts and components.
- Toxoplasma gondii serological reagents.
- Rheumatoid factor immunological test systems.
- Calibrators for hemoglobin or hematocrit measurement.
- Immunoglobulins A, G, M, D, and E immunological test systems.

Q. Why should FDA support voluntary standards?

A. Existing national and international voluntary standards programs contribute significantly to the development of medical device standards. In many cases, the most efficient use of resources may be a joint effort by industry and government representatives in writing consensus standards to which manufacturers would voluntarily conform. The approach encourages cooperation and allows full participation of nongovernment interests. It does not, however, remove the need for mandatory standards.

Q. How is a mandatory standard developed?

A. The law requires a 5-step process to be announced in the *Federal Register* as follows:

- A notice announces the opportunity for interested persons to request that the device be reclassified from class II to class I or class III.
- If the device is not reclassified, a notice invites interested persons or organizations to submit an existing standard or to offer to develop a standard.

- Upon receiving any offers, FDA may accept an existing standard, accept an offer to develop a standard, or proceed on its own in developing a standard.
- An announcement explains the proposed standard and requests comments. Any technical or scientific issues may be referred to an independent standards advisory committee.
- Upon resolution of any technical or scientific issues, FDA publishes the standard as a final regulation to become effective in one year. FDA is actively working on a mandatory standard for breathing frequency (apnea) monitors.

Q. Must clinical trials ever be conducted in support of the safety and effectiveness of a class II device? If so, must an Investigational Device Exemption (see section VI) be obtained?

A. Clinical trials may be needed to establish that a given class II device is as "safe and effective" as the marketed device to which "substantial equivalence" is claimed. Also, clinical trials may be required to establish a new use of an "old" device. However, the IDE regulation exempts a clinical investigation on a marketed device when the investigation involves one of the labeled indications for use.

V. Premarket Approval

A. General Guidelines (Section 515)

Class III devices are subject to the premarket approval requirements of section 515 of the FD&C Act. Similar to a new drug approval, an approved Premarket Approval Application is, in effect, a private license granted to the applicant to market a particular medical device. The requirements for premarket approval apply differently to pre-amendment devices, to post-amendment devices, and to "transitional" devices (devices regulated as new drugs or antibiotic drugs before May 28, 1976).

A pre-amendment device is a device that was in commercial distribution before the May 28, 1976, enactment date of the Amendments. The manufacturer of a class III pre-amendment device cannot be required to submit a PMA until 30 months after the effective date of a final classification regulation or until 90 days after publication of a final regulation requiring the submission of a PMA, whichever period comes last. The PMA must contain valid scientific evidence showing that there is reasonable assurance of the safety and effectiveness of the device under its conditions of use.

A post-amendment device is a device put in commercial distribution after May 28, 1976. (See page 13 for a complete definition of commercial distribution.) A post-amendment device that is substantially equivalent to a pre-amendment class III device is subject to the same requirements. FDA determines substantial equivalence after reviewing the manufacturer's premarket notification submitted in accordance with section 510(k) of the FD&C Act. A post-amendment device that is not substantially equivalent to a pre-amendment device is automatically in class III and must undergo premarket approval or be reclassified into class I or class II before it can be marketed.

Class III "transitional" devices and "new" devices (post-amendment devices that are not substantially equivalent to pre-amendment devices or to class I or class II post-amendment devices) are automatically classified into class III by statute and require premarket approval by FDA before marketing. Manufacturers of these devices may either submit a PMA or petition FDA to reclassify the devices into class I or class II. Clinical studies in support of a PMA or a reclassification petition are subject to the IDE regulation. (See section VI, "Exemption for Devices for Investigational Use.")

Through administrative review, FDA determines whether the PMA includes the required information and whether it is suitable for filing. An incomplete PMA is not considered to be filed until it is resubmitted and is accepted for filing. If the PMA is suitable for scientific review, the filing date is the date FDA received the complete PMA, and the 180-day review period provided by the FD&C Act begins on this filing date. Substantial changes may "restart" the "clock" when

a new (amended) PMA is filed. Once accepted for filing, the PMA undergoes scientific review by appropriate FDA personnel and advisory committee(s). FDA promptly notifies PMA applicants of any apparent deficiencies. After receiving recommendations from the advisory committee, FDA approves or denies a PMA within the 180-day review period unless FDA and the applicant have agreed to a longer period. FDA notifies the applicant of its decision by letter. A *Federal Register* notice is then published announcing the decision and the availability of a summary of the safety and effectiveness data on which the decision is based. The notice also provides the applicant and other interested persons an opportunity for administrative review of the FDA approval or denial action.

Q. Does FDA offer informational and other materials to assist industry in developing and assembling a PMA?

A. Yes. CDRH furnishes a number of aids including a PMA manual and "Guideline for the Arrangement and Content of a Premarket Approval Application." These may be obtained from the Program Management Staff, Office of Device Evaluation, CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850 (301-427-1186) or DSMA (800-638-2041). Related materials for use in assembling a PMA are also available upon request from DSMA (800-638-2041).

Q. Has a section 515(b) regulation requiring a PMA submission for pre-amendment devices been published in the *Federal Register?*

A. FDA proposed a rule requiring the filing of a premarket approval application for the implanted cerebellar stimulator in the *Federal Register* of September 6, 1983. It also published a list of pre-amendment devices that have high priority for requirement of PMA filing.

Several pre-amendment PMAs have been called for since. There is a lengthy regulatory process involved. On January 6, 1989, FDA published a notice of advanced intent to establish the effective date of the requirement for Premarket Approval for 31 class III pre-amendment devices. Pre-amendment PMAs cannot be required until after 30 months following the final classification regulation, or until after 90 days following printing of the regulation calling for a specific device PMA, whichever time period comes last. If no PMA is yet required, the manufacturer can submit a premarket notification for a pre-amendment class III device. However, the firm should be prepared to submit data to support a PMA filing when required.

For more information on 515(b) filings, call the Office of Device Evaluation (301-427-1186) or DSMA (800-638-2041).

Q. Must evidence of both safety and effectiveness be included in a PMA for class III pre-amendment devices and for devices determined by FDA to be their substantial equivalent?

A. Each PMA must contain evidence about both safety and effectiveness. Sometimes, safety and effectiveness data on the device may be available in the literature. In such instances, the literature can be cited rather than submitted in the PMA itself. Requirements for data will be determined on an ad hoc basis.

Q. Can a product that has received approval under a PMA be advertised as "FDA approved?"

A. No. Reference to premarket approval, investigational device approval, or any report or analysis resulting from an inspection are prohibited by sections 301(l) and (n) of the Act. In addition, reference to establishment registration or a registration number may be misleading and result in the misbranding of a device according to the registration regulation (21 CFR 807.39).

In general, manufacturers should avoid any representation that creates an impression of official approval of a device because of compliance with the FD&C Act or an FDA regulation.

B. Product Development Protocol [Section 515(f)]

Section 515(f) of the FD&C Act authorizes an alternative to the IDE/PMA premarket approval process for a class III device—the Product Development Protocol (PDP). Requirements for proof of safety and effectiveness are as stringent under the PDP as they are under the PMA approach. The major distinguishing feature of the PDP is FDA's early involvement at the design or preclinical testing phase. FDA and the appropriate advisory committee work closely with the sponsor in designing suitable preclinical tests and clinical investigations to establish the device's safety and effectiveness. The PDP has proven to be rarely feasible for a manufacturer and overly demanding of FDA resources. Similar but less formal consulting services are available for anyone planning a PMA submission. Call DSMA (800-638-2041) if you need assistance.

Q. Does the manufacturer have any legal recourse if FDA determines that a PDP is inappropriate and refuses to accept the PDP?

A. No. This decision is at FDA's discretion.

VI. Exemption of Devices for Investigational Use

Section 520(g) of the FD&C Act authorizes FDA to exempt devices intended solely for investigational use from certain requirements of the FD&C Act in order to allow for their shipment and use on human subjects. This provision applies to investigational studies undertaken to develop safety and effectiveness data for a medical device when these studies use human subjects. An applicant for an Investigational Device Exemption (IDE) for a "significant risk" device must submit information to demonstrate that the testing will be supervised by an Institutional Review Board (IRB), that appropriate informed consent will be provided, and that certain records and reports will be maintained. Submission of an IDE to FDA is not required for a "nonsignificant" risk device.

The FDA conducts a bioresearch monitoring program involving inspections of sponsors, clinical investigators, IRBs, and non-clinical laboratories to assure validity of scientific data and compliance with IDE requirements.

Q. Are devices with an approved IDE exempt from section 501 on adulteration or section 518 on notification and other remedies?

A. No. An investigational device may be considered adulterated under section 501(i) if the sponsor or investigator fails to comply with a requirement of the IDE regulation (21 CFR part 812). Section 518 is applicable, however, only to devices in commercial distribution, and since investigational devices are not to be commercialized, section 518 is not relevant to devices with an approved IDE.

Q. Who decides whether a given device poses a "significant risk" as that term is used in the IDE regulation?

A. The local IRB decides whether or not a device proposed for clinical testing under its review will expose patients to a "significant risk." If so, FDA must approve the study. If not, the investigator may proceed without notifying FDA, but must comply with the sections of the IDE regulation applicable to non-significant risk devices. If the study comes to the attention of the FDA for some reason, FDA can overrule the IRB decision.

Q. Are custom devices exempt from the IDE regulation?

A. Yes, if the devices are not being tested to determine safety or effectiveness for purposes of commercial distribution. Custom devices are subject to all provisions of the FD&C Act except sections 510(k), premarket notification; 514, performance standards; and 515, premarket approval.

Q. Are devices in commercial distribution before May 28, 1976, exempt from IDE requirements?

A. In general, yes. The IDE regulation exempts pre-amendment devices, other than "transitional" devices, if they are used or investigated in accordance with labeling in effect before May 28, 1976. For class II devices, this exemption expires on the effective date of a regulatory performance standard. If the devices do not meet the performance standard, they may be distributed only under an approved IDE. For class III pre-amendment devices, this exemption expires 90 days after the effective date of the FDA regulation or order calling for a PMA submission.

Q. Are all devices marketed after May 28, 1976, subject to the IDE regulation?

A. Except for "transitional" devices, the IDE regulation exempts post-amendment devices that FDA has determined to be substantially equivalent to pre-amendment devices if they are tested for claims made in the labeling that FDA reviewed when determining substantial equivalence.

Q. Must a sponsor ask FDA whether a device is substantially equivalent to a pre-amendment device before initiating a clinical investigation?

A. No, the local IRB may decide that the device does not pose a "significant risk" to patients. Since a device can be exempt if it is substantially equivalent, FDA encourages checking for equivalence first. This check may prevent a sponsor from spending money and effort for clinical studies of substantially equivalent devices. Information required in 510(k) submission is described in 21 CFR 807.87.

Q. If a radiation-emitting investigational device is subject to the IDE regulation, is it also subject to the radiological health device regulations?

A. An IDE grants exemption from certain provisions of the FD&C Act; it does not grant exemption from other Federal, State, or local regulations. Certain radiation-emitting electronic products may also be investigational medical devices; these are subject to radiological health device regulations, e.g., product performance standards for products such as lasers and diagnostic x-rays. Under these regulations, however, some variances may be granted. Such variances must be applied for separately under CDRH procedures.

Q. Is a device that introduces energy into a subject's body a significant risk device?

A. Such a device may be a significant risk device. However, the risk rating depends on the condition of the patient, conditions of use, device purpose, and power output.

Q. Is it possible for a device implanted for less than 30 days to be a significant risk device?

A. Yes. FDA may declare such a device to be a significant risk device, but the determination would be made on a case-by-case basis. The decision whether a product involves significant risk depends on the intended use of the device rather than on its nature as an implant.

Q. If a device has several uses, one of which involves significant risk, are investigations of the nonsignificant risk uses subject to the significant risk requirements of the IDE regulation?

A. No. It is subject only to those sections of the IDE regulation applicable to nonsignificant risk devices. If that same device is used in an investigation that presents significant risk, it is subject to the full IDE requirements for that use.

Q. What kind of testing is exempt from the IDE regulation?

A. The following testing is exempt:

- Consumer preference testing of devices, testing of a modification, or testing of a combination of two or more devices in commercial distribution if the testing is not to determine safety and effectiveness and does not put subjects at risk.
- Research testing for purposes other than determining the safety and effectiveness of a device for human use.
- Testing of devices (1) that are legally in commercial distribution if the testing accords with the indications in the device's labeling; (2) that are intended solely for veterinary use; or (3) that are shipped solely for research with laboratory animals and are labeled appropriately.
- Testing of diagnostic devices that comply with diagnostic device labeling requirements under 21 CFR 809.10 and that meet exemption criteria in 812.2(c)(3).

In addition, the IDE regulation does not apply to fabrication of a custom device if the device is not being tested to determine safety and effectiveness for purposes of commercial distribution or to an intraocular lens subject to an approved IDE under 21 CFR part 813.

Q. Where can I learn more about the IDE regulation?

A. Call or write the Program Management Staff, Office of Device Evaluation, CDRH, FDA (HFZ-420), 1390 Piccard Drive, Rockville, MD 20850 (301-427-1190) or DSMA (800-638-2041). An IDE manual for manufacturers is available from these sources.

VII. Custom Devices

Custom devices are those devices that may be ordered by custom devices physicians or dentists for their own use or for patients, are not generally available in finished form, and are not labeled or advertised for commercial distribution.

Under section 520(b), custom devices are exempt from otherwise applicable performance standards or premarket approval requirements as well as premarket notification. This exception applies only to devices that are not generally available in finished form for dispensing, prescription, or commercial distribution. In addition, custom devices must not be generally available to other licensed practitioners. Except for premarket notification, such devices must comply with all general control requirements relating to GMPs, investigational use of devices, banning, restriction, adulteration, and misbranding.

Traditionally, the FDA has interpreted the term "custom device" very strictly; *most* devices claimed to be "custom" by the manufacturers have been determined not to be custom devices by FDA.

Q. What is the definition of a custom device?

A. The IDE regulation [21 CFR 812.3(b)] defines a custom device as follows: "custom device" means a device that:

- Necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order of an individual physician or dentist;
- Is not generally available to, or generally used by, other physicians or dentists;
- Is not generally available in finished form for purchase or for dispensing by prescription;
- Is not offered for commercial distribution through labeling or advertising; and
- Is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

Q. What is meant by the term "generally available" mentioned above?

A. A custom device may not be offered for general commercial distribution; i.e., off-the-shelf. It should not, for instance, appear in any catalog. It is specifically tailored to meet the needs of one health professional in his practice or for the needs of his patient. If there is any question whether or not a device is a custom device, advice should be obtained from the Office of Compliance and Surveillance (HFZ-340), CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850 (301-427-1144).

Q. Are manufacturers of custom devices subject to registration?

A. Yes. The statutory language and the legislative history make it clear that a custom device must meet all the requirements of the Act except those imposed by or under section 510(k) (premarket approval), 514 (performance evaluation), and 515 (premarket approval).

VIII. Preemption of State and Local Requirements

Section 521(a) of the FD&C Act preempts State and local requirements for devices that differ from or are in addition to those established by FDA. When State or local device laws and regulations are preempted, the State may petition FDA under section 521(b) for an exemption of this preemption. FDA may exempt a State or local device requirement (1) if the State requirement is more stringent than a requirement of the FD&C Act or (2) if exemption is required by compelling local conditions, and devices that comply with the State or local requirement will not be in violation of the FD&C Act.

Q. May a State establish criteria governing who is qualified to dispense medical devices, e.g., registered pharmacists dispensing drugs?

A. Yes. FDA recognizes that there is a difference between a State's product-related requirements (which could be preempted unless FDA provides otherwise upon application by the State) and professional licensing-related requirements (which are not preempted by Federal regulation).

Q. Will FDA routinely exempt State device programs from the preemption provision of the FD&C Act?

A. No. FDA will consider a properly submitted application to exempt such State programs from this preemption provision. FDA will not, however, routinely exempt State requirements that meet only the minimum conditions established by law for such an exemption. FDA will also consider whether the public health will benefit if an exemption is granted.

IX. Inspections Relating to Devices

Section 704 of the FD&C Act authorizes FDA to inspect establishments manufacturing or holding medical devices. Under new section 704(e), FDA now has clear authority to inspect and copy any records required under sections 519 or 520 (f). Refusing to allow FDA to inspect or copy any record required by this regulation, or causing such a refusal, is prohibited under section 301(e).

Q. How and under what priorities are manufacturers selected for inspectional coverage?

A. Several criteria are used including type of device, size of firm, and history of recent problems with the firm or its products. FDA is mandated by law to inspect all manufacturers of class II and class III devices at least once every two years. Because of the high patient risk involved in using critical medical devices, however, FDA is especially interested in visiting manufacturers that distribute or produce large numbers of these devices for health care facilities. If FDA receives complaints about such critical devices, these manufacturers will be given highest inspectional priority. Reported problems with class III and class II noncritical devices distributed in large numbers also will result in priority attention to these manufacturers. Generally, class I device manufacturers receive lowest priority for GMP inspection.

Q. What to FDA investigators look for during a GMP inspection?

A. FDA has developed and implemented compliance program 7378.830, "Inspection of Medical Device Manufacturers," to determine the extent to which manufacturers are complying with the device GMP regulation and are producing devices fit for intended use. Investigators determine whether the manufacturer complies with applicable GMP requirements by reviewing and evaluating records, labeling procedures, specifications, and equipment, and by observing operations and personnel.

Inquiries regarding FDA inspections or investigator responsibilities should be directed to your local FDA district office. (See Appendix B, "FDA District Offices.")

The FDA Device Compliance Program may be purchased from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Rd., Springfield, VA 22161. Call

DSMA to obtain the NTIS Accession Number, as it changes with each new compliance program.

Q. How is a device selected for coverage during an inspection?

A. Investigators select enough class II or III devices in an establishment to cover the "profile classes" used in that establishment.

Q. What is a "profile class"?

A. The term "profile class" refers to general processes such as metal fabrication, plastic or rubber fabrication, and electronic assembly, among others. The term is derived from the Government-Wide Quality Assurance Program.

Q. What is the Government-Wide Quality Assurance Program?

A. This program is an approach in which the FDA (for example) signs agreements with other government agencies such as the Department of Defense or the Veterans Administration to make required inspections of medical device manufacturing establishments to obviate duplicative inspections.

Q. Is the information contained in an investigator's Establishment Inspection Report (EIR) available to the public?

A. Yes. Most information in the EIR of a completed investigation may be released to the public under the Freedom of Information Act. An EIR related to an ongoing investigation is not available for public disclosure until the investigation is closed. The Freedom of Information Act also protects from public disclosure all confidential and trade secret information in these reports. (See section X, "Trade Secrets.")

Q. What is the significance of receiving a Notice of Adverse Findings Letter?

A. FDA sends such a letter to a manufacturer to assure that top management is aware of significant deficiencies revealed by an inspection. This is intended to effect prompt correction of the violative product and/or condition; the letter generally requests a response within 30 days.

Q. What is the significance of a Regulatory Letter?

A. FDA sends a regulatory letter to a manufacturer when serious deficiencies or problems exist in that manufacturer's products or establishment and when the manufacturer has not taken prompt and effective action to correct such problems. A regulatory letter is an administrative action taken by FDA in lieu of a regulatory action such as a seizure or injunction. A regulatory letter means that FDA is prepared to take regulatory action if a firm does not correct a problem within a reasonable period of time. A regulatory letter generally requests a firm to respond within 10 days. If the firm fails to respond or its response is inadequate, FDA may initiate a legal action.

Q. Should a manufacturer always reply in writing to a form FD-483 left by an investigator at the conclusion of many inspections?

A. This is left to the discretion of the manufacturer. A written response is usually a good idea since it presents the manufacturer's side of the findings and becomes a part of the firm's record. A written response also reflects the manufacturer's concern with correcting or resolving the findings.

X. Trade Secrets and Confidential Information

Sections of the Amendments concerning the confidentiality of information are intended to protect trade secrets and to prohibit their use to a competitor's advantage. These provisions also give the public the right to information necessary to assess the propriety of FDA actions with respect to devices. Although a manufacturer may indicate the he/she regards certain information submitted under the provision of the FD&C Act a trade secret, FDA makes the final determination of what is or is not a trade secret. Essentially, FDA bases this determination on the concept of competitive advantage, i.e., if knowledge about device characteristics would give the possessor of such knowledge the opportunity for an advantage over competitors who do not know the characteristics.

Section 520(c) prohibits FDA from using trade secret information as the basis for reclassifying a device from class III to class II or for establishing or amending a performance standard for a device so reclassified. To ensure proper public scrutiny of FDA device-related actions, section 520(h) requires FDA to disclose a detailed summary of the safety and effectiveness information that served as a basis for major decisions concerning a device. Such summaries must include information on any adverse health effects of the device.

Section 301(j) makes it a criminal act for anyone to use to his/her own advantage or to disclose (other than to the courts) trade secret information submitted to FDA. The critical issue for the purposes of section 301(j), however, is the determination of what constitutes a trade secret. For class I or class II devices, except for material previously disclosed to the public, any safety and effectiveness data submitted to a classification panel is considered confidential until a decision on final classification is reached.

Under section 708, FDA may release trade secret information to a contractor who requires this information for an activity contracted with FDA. The release of trade secrets and other confidential information to contractors must be contingent upon the contractor's implementation of prescribed security precautions.

Q. Has FDA published its rules and intent for handling confidential information?

A. FDA's policy and procedures on public information disclosures are outlined in 21 CFR part 20. The kind of information available to the public from an investigator's EIR is specifically listed in 21 CFR 20.64 and in 21 CFR 20.101.

Q. What is a trade secret?

A. A trade secret may consist of any formula, pattern, device, or compilation of information used in one's business which gives the manufacturer an opportunity tc obtain an advantage over competitors who do not know or use it (21 CFR 20.61).

Q. What is "Confidential Commercial or Financial Information?"

A. Confidential commercial or financial or financial information is valuable data or information used in one's business that the manufacturer customarily holds in strict confidence or regards as privileged and does not disclose to any member of the public.

Q. Will FDA notify a manufacturer before any information marked "confidential" is released under the Freedom of Information Act (FOI)?

A. Yes, but only under limited circumstances. FDA will provide submitters of premarket notification 510(k) submissions and reports received under the Radiation Control for Health and Safety Act with such notification, the first time that an FOI request is received for these data. The firm is then provided with the opportunity to indicate what portions of the submission(s) should not be publicly released because the data falls within the exemptions provided by the Freedom of Information Act. In all other circumstances, FDA will determine the trade secret status by the inherent nature of the material, rather than the designation provided by the person submitting it to FDA. Records submitted to FDA marked "confidential" or other similar terms do not obligate FDA to regard them as confidential, to return them to the sender, to withhold them from disclosure to the public, or to advise the person submitting them when a request for their public disclosure is received or when they are in fact disclosed.

Q. Are premarket notifications available for public disclosure under the FOI act?

A. Yes. Such submissions are available when the intent to market the device is known, after the deletion of trade secret and confidential commercial information. Submissions that are still under FDA review, or those for which the submitting firm has requested continuing confidentiality, may not be publicly disclosed. To assure confidentiality, the submitting firm should provide written certification to FDA that the submission is to be considered completely confidential until the intent to market is known (i.e., until the firm advertises or publicly acknowledges the existence of the submission). (See 21 CFR 807.95.)

Q. Will a company have access to information compiled on its device through FDA's Device Experience Network?

A. Yes. Any information released by FDA, however, will not disclose the identity of the individual patient, health professional, or institution submitting the report. FOI requests may be addressed to: Freedom of Information Office (HFI-35), FDA, 5600 Fishers Lane, Rockville, MD 20857.

Q. What is the Device Experience Network?

A. The Device Experience Network (DEN) is a computer data base that contains reports collected from health care professionals on various problems with medical and in vitro diagnostic products.

This information system collects, stores, and retrieves these problem reports. The DEN system is operated by the Device Monitoring Branch, Division of Product Surveillance, CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850 (301-427-1144). If you wish to report a defective device, write that address or phone (toll free) 800-638-6725. In Maryland, you must call collect, 301-881-0256.

The objective of the DEN system is to aid the protection of the public health by:

- Collecting and evaluating all device experience information;
- Identifying hazardous devices, industry-wide problems, and significant trends; and
- Providing information that may help to improve design, quality, and use of medical devices.

XI. Traceability

Through past experiences with the regulation of potentially hazardous devices, FDA recognizes that the ability to trace a device through various channels of commercial distribution can be a valuable regulatory tool for protecting the public health. FDA is also aware, however, that such traceability can be extremely expensive and is often unnecessary for some devices, especially for those unlikely to pose a health hazard. Thus, FDA attempts to differentiate between devices for which traceability is and is not necessary to protect the public health. Under the GMP regulation, critical devices must be traceable (21 CFR 820).

Q. Are manufacturers currently required to report every corrective field action, such as recall, to FDA?

A. No, except for medical devices subject to PL 90-602 (Radiation Control for Health and Safety Act). Manufacturers are requested, but not required, to report voluntary recalls to FDA.

Q. With the possibility of increased product liability cases, will FDA personnel be allowed to testify in private suits brought against manufacturers?

A. Not usually. On rare occasions, the Commissioner of FDA may grant special approval for an individual employee if he believes the litigation will further the general intent of the FD&C Act.

XII. Assistance for Small Manufacturers of Devices

To aid small manufacturers in complying with device regulations, a Division of Small Manufacturers Assistance (DSMA) exists in the Office of Training and Assistance of CDRH. In passing the Amendments in 1976, Congress was impressed with the difficulties that smaller firms with limited resources might have in understanding and obeying the pertinent laws and regulations as well as in bearing the cost involved. As a result, it included section 10 relating to the amended FD&C Act, calling for "... an identifiable office to provide technical and other nonfinancial assistance to small manufacturers to assist them in complying" with the FD&C Act. As mandated, an office of assistance for small manufacturers, DSMA, was established. DSMA is a fully functional arm of CDRH; its mission is to aid the small manufacturer in complying with the law and to clarify the requirements of medical device regulations.

Q. How does DSMA aid small firms?

A. DSMA provides assistance in five distinct areas:

- *Response to small manufacturer inquiries.* DSMA's staff of FDA specialists is thoroughly knowledgeable about FDA device laws and regulations and provides accurate and complete responses to inquiries from small manufacturers. Such requests for information may be made by phone of letter; on occasion, industry representatives visit the DSMA office directly for assistance.
- *Printed materials.* DSMA distributes a wide range of printed materials, including publications developed by DSMA and other CDRH offices, and *Federal Register* documents such as policy statements, guidelines, and proposed and final regulations. DSMA's major publications are series of manuals developed for DSMA workshops. These manuals also are available for sale from the U.S. Government Printing Office, Washington, D.C. 20402 (202-783-3228). To order publications or to obtain an order form, call DSMA at 800-638-2041.
- *On-site visits.* By invitation DSMA representatives visit device manufacturing facilities to provide first-hand advice and assistance. They are prepared to informally audit the firm's compliance with FDA manufacturing controls and to provide advice on how compliance can be achieved.
- *Workshops.* DSMA holds workshops at regional locations nationwide. These provide an

opportunity for small firms to meet at a convenient location with representatives of DSMA and other FDA officials, to keep current on compliance matters, to obtain authoritative responses to their inquiries, and to express their concerns.

Specific day-long workshops have been developed on "Regulatory Requirements for Marketing a Device," "The GMP Regulation," "Sterile Devices," "Import-Export Requirements," "Clinical Concepts," "In Vitro Diagnostic Devices," and "Process Validation and Preproduction."

Other subjects may be added when the need is indicated.

For workshop information, contact DSMA (800-638-2041).

- *Regulatory Overview.* As spokesman for small manufacturers, DSMA reviews and comments on drafts of proposed and final regulations, policy statements, and guidelines as to whether they are unduly burdensome, stifle innovation unnecessarily, or place the small manufacturer at a competitive disadvantage. DSMA encourages small manufacturers to comment on proposed regulations and to seek appointment to FDA advisory committees.

XIII. Import and Export of Devices

A. Imports [Section 801(a), (b), and (c)]

Devices and accessories, in either a finished or semi-finished state, must comply with applicable U.S. regulations before being imported for distribution. Imported devices that do not meet these requirements are subject to detention by FDA at the port of entry.

A premarket notification submission is not required if the foreign manufacturer's product was previously reviewed by FDA and found to be equivalent under section 510(k) or if it was distributed by other firms in the U.S. prior to the enactment date of the Amendments, May 28, 1976. A device determined to be substantially equivalent to one already in the U.S. market has the same classification as that device and is subject to all the requirements of that class. This applies whether the device being marketing was first distributed before or after the enactment date of the Amendments, May 28, 1976.

Pre-amendment devices classified into class III must undergo premarket approval in accordance with section 515 of the FD&C Act (see section V). FDA can require the submission of a PMA 30 months after the final classification of the device into class III. After this final classification, the initial distributor or foreign manufacturer should use the 30-month period to develop data supporting the device's safety and effectiveness. It is important to note that 30 months after the date of final classification is the earliest the FDA can require a PMA. FDA may actually call for such applications much later, depending on agency priorities.

Q. What is expected of foreign manufacturers whose devices are subject to premarket approval?

A. All premarket approval requirements are applied equally to both foreign and domestic manufacturers. Whether conducted in the United States or abroad, studies to acquire PMA data must be performed according to the regulations established for the investigational use of devices (see section VI, above). FDA reviews the PMA to determine whether the submitted data is sufficient to demonstrate the device's safety and effectiveness.

Q. What are the registration and listing requirements for imported devices?

A. Foreign manufacturers of devices imported into the United States are requested, but not required, to register their establishments. They must list their imported devices with FDA, or they may authorize an initial distributor to complete the listing form FDA-2892 on their behalf. An initial distributor so designated must be the sole initial distributor of the devices listed and must maintain the listing historical file for the devices (section 510, FD&C Act).

All initial distributors of imported medical devices must register with FDA. They must comply with device listing by identifying to FDA those foreign firms whose devices they import. In addition, an initial distributor that either develops specifications for the foreign-manufactured device or further repackages and/or relabels the device after receipt from the foreign firm must list the device by submitting form FDA-2892.

Q. Will FDA conduct inspections of foreign manufacturers?

A. Yes. FDA anticipates that onsite inspections of foreign manufacturers will continue to be conducted. Foreign manufacturers are requested to provide FDA investigators with access to information on manufacturing processes, quality control activities, and distribution, and data on research and testing.

Q. What are the primary grounds for detention or refusal of admission of imported devices?

A. Primary grounds for detention or refusal of admission are:

- The initial distributor of the device has not registered and/or the device has not been listed either by the foreign manufacturer or by the firm's authorized representative.
- It appears from examination of the shipment or the shipment samples (or otherwise) that the methods used in, or the facilities and controls used for, the manufacture, packing, storage, or installation of the device do not comply with the GMP regulation.
- The device cannot be sold, or sale is restricted, in the country of origin.
- The device is otherwise adulterated or misbranded.

B. Exports [Section 801(e)]

Devices commercially marketed in the United States can be exported if they meet the requirements of the consignee's country, e.g., if they are labeled in the appropriate foreign language. Devices intended for export only will not be considered adulterated or misbranded if the following four requirements are met:

- They meet with the specifications of the foreign purchaser,
- They are not in conflict with the laws of the country to which they are intended for export,
- The label on the outside of the shipping package states that the devices are intended only for export, and
- They are not sold or offered for sale in domestic commerce.

Some devices that are not in commercial distribution in the U.S. may still be exported if (1) they meet the above four conditions, (2) FDA determines that exporting the devices would not be contrary to the public health and safety of the country intended to receive them, and (3) FDA receives notices of the approval of that country. Such devices include:

- Banned devices.
- Devices subject to an IDE.
- Devices that have never been marketed in the United States and are without an acceptable premarket notification [510(k)].
- Class II devices that do not adhere to applicable domestic (FDA) performance standards.
- Class III devices that do not have either an approved PMA, PDP, or IDE.

Q. Must manufacturers of exported devices register with FDA?

A. Yes. All domestic device manufacturers, including those whose products are intended for export only, must register their establishments and list their devices with FDA.

Q. How does FDA handle recalls involving exported devices?

A. Through worldwide foreign service posts, FDA's Office of International Affairs notifies foreign countries of all recalls involving exported devices. The importing country may return recalled devices when necessary.

Q. Does FDA issue a "Certificate of Free Sale" for devices for export?

A. No. A factual statement of the status of a specific device subject to FDA jurisdiction may be provided upon request. Under special circumstances, this statement may be obtained as a certified copy issued by the Department of Health and Human Services. For details, contact the Office of Compliance and Surveillance (HFZ-320), CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850 (301-427-1116) or call DSMA (800-638-2041).

Q. Under what circumstances does FDA require written permission from the government of a foreign country where unapproved domestic products are offered for export?

A. This is required if the devices are banned, do not meet applicable performance standards, do not meet premarket approval requirements, or for any reason are not approved for marketing in this country.

Q. Could a manufacturer be required to contact more than one FDA office concerning an import/export?

A. Yes. There are sometimes several Offices or Centers involved with certain devices due to overlapping jurisdictions. For example, some devices fall within the jurisdiction of both CDRH and the Center for Drug Evaluation and Research. To determine whether a device is subject to more than one office, contact the Division of Product Surveillance (HFZ-340), CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850 (301-427-1144) or call DSMA (800-638-2041).

Q. Where can I obtain my import/export information?

A. Contact the Office of Compliance and Surveillance (HFZ-320), CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850 (301-427-1116) or call DSMA (800-638-2041).

XIV. Color Additives for Devices

The Medical Device Amendments of 1976 amended section 706 of the FD&C Act to make certain color additives in devices subject to the same provisions that apply to color additives in foods, drugs, and cosmetics. CDRH plans to issue guidance on color listing obligations of device manufacturers.

The FD&C Act provides that devices containing color additives are adulterated unless a regulation is in effect listing the color for such use. A "listing" regulation identifies a color and prescribes a specific use, either in general or in narrow terms. The Act limits applicability of these provisions to color additives that directly contact the body for a significant period of time.

Q. What is FDA's definition of "a significant period of time?"

A. At the present time, there is not identification for the term "a significant period of time." This phrase, however, may be clarified in future regulations. Meanwhile, manufacturers must use their discretion in this area.

Q. How should a manufacturer proceed with respect to the use of color additives in or on devices?

A. Until proposed or final regulations are published by FDA, manufacturers may obtain approval to use or to investigate a color additive in or on a device through a color additive petition (as provided in 21 CFR part 71).

Devices subject to premarket approval and containing a color additive will not be approved until the color is listed. A color listing enforcement policy has not been adopted for 510(k) reviews because these reviews end with a substantially equivalent judgment, not with an FDA approval. Manufacturers seeking to add a new color additive to a device should submit a premarket notification [510(k)] to FDA. They may want to consult with FDA to determine which approach to use and what type of data they will have to submit. For more information contact the Division of Product Surveillance (HFZ-340), CDRH, FDA, 1390 Piccard Drive, Rockville, MD 20850 (301-427-1144) or call DSMA (800-638-2041).

XV. Medical Device Reporting

Since December 13, 1984, a new regulation, Medical Device Reporting (MDR), requires that a manufacturer or importer (initial distributor) report whenever they become aware of information that reasonably that one of their marketed devices:

(1) May have caused or contributed to a death or serious injury; or
(2) Has malfunctioned, and if the malfunction were to recur, the device or any other device marketed by the firm would likely cause or contribute to a death or serious injury.

Reports of *death or serious injury must be telephoned* to FDA at 301-427-7500 no later than *five (5) calendar days* from the time the manufacturer or initial distributor (importer) receives the information. In addition to the telephone report requirement, manufacturers and initial distributors must send a *written report to FDA within 15 working days* from the time the firm or person receives information *for all reports of:*

(1) Death or serious injury, or;
(2) Malfunction likely to cause or contribute to death or serious injury.

An added initial distributor requirement: Under MDR, the initial distributor/importer is required to establish and maintain a complaint file and to permit any authorized FDA employee, at all reasonable times, to have access to and be able to copy and verify, the records in the file.

Q. What does FDA consider a complaint?

A. As stated earlier, FDA considers a "complaint" to be *any* expression of dissatisfaction, be it oral or written, regarding the identity, quality, durability, reliability, effectiveness, or performance of a device.

Q. How do I know if an incident is reportable under MDR?

A. CDRH has a guidance publication which explains this regulation, *Medical Device Reporting; Questions and Answers.* For answers to general questions about MDR, contact DSMA (800-638-2041). For specific questions as to whether a given situation must be reported, call 301-427-1156. Address written MDR reports and inquiries to:

Center for Devices and
Radiological Health
Division of Product Surveillance
Device Monitoring Branch
HFZ-343
1390 Piccard Drive
Rockville, MD 20850

APPENDIX A
Classification (Advisory) Panels

Anesthesiology and Respiratory Therapy	427-1044
Circulatory Systems	427-1205
Clinical Chemistry and Clinical Toxicology	427-1096
Dental	427-1180
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Gastroenterology and Urology	427-1220
General and Plastic Surgery	427-1036
General Hospital and Personal Use	427-1225
Hematology and Pathology	427-1096
Immunology	427-1096
Microbiology	427-1096
Neurology	427-1053
Obstetrics and Gynecology	427-1180
Ophthalmic	427-1072
Orthopedic and Rehabilitation	427-1036
Radiology	427-1050

Note: Food and Drug Administration, CDRH, 1390 Piccard Drive, Rockville, MD 20850. Area code for all telephone numbers is 301.

APPENDIX B
FDA District Offices

District	States Served
Atlanta 60 Eighth Street, N.E. Atlanta, Georgia 30309 Phone: (404) 347-3151	Alabama, Georgia, North Carolina, South Carolina
Baltimore 900 Madison Avenue Baltimore, Maryland 21201 Phone: (301) 962-4099	District of Columbia (D.C.), Maryland, Virginia, West Virginia
Boston One Montvale Avenue Stoneham, Massachusetts 02180 Phone: (617) 279-1478	Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont
Buffalo 599 Delaware Avenue Buffalo, New York 14202 Phone: (716) 846-4480	New York (Upstate)
Chicago 1222 Post Office Building 433 West Van Buren Street Chicago, Illinois 60607 Phone: (312) 353-7769	Illinois
Cincinnati 1141 Central Parkway Cincinnati, Ohio 45202 Phone: (513) 684-3501	Ohio

District	State Served
Dallas 3032 Bryan Street Dallas, Texas 75204 Phone: (214) 655-5310	New Mexico, Oklahoma, Texas
Denver Building 20 Denver Federal Center P.O. Box 25087 Denver, Colorado 80225 Phone: (303) 236-3050	Colorado, Montana, North Dakota, South Dakota, Utah, Wyoming
Detroit 1560 East Jefferson Detroit, Michigan 48207 Phone: (313) 226-2253	Indiana, Michigan
Kansas City 1009 Cherry Street Kansas City, Missouri 64106 Phone: (816) 374-6376	Iowa, Kansas, Missouri, Nebraska
Los Angeles 1521 West Pico Boulevard Los Angeles, California 90015 Phone: (213) 252-7599	Arizona, California (Southern)
Minneapolis 240 Hennepin Avenue Minneapolis, Minnesota 55401 Phone: (612) 334-4120	Minnesota, Wisconsin
Nashville 297 Plus Park Boulevard Nashville, Tennessee 37217 Phone: (615) 736-5852	Kentucky, Mississippi, Tennessee

District	State Served
Newark 61 Main Street West Orange, New Jersey 07052 Phone: (201) 645-6234	New Jersey
New Orleans 4298 Elysian Fields Avenue New Orleans, Louisiana 70122 Phone: (504) 589-6345	Arkansas, Louisiana
New York 850 Third Avenue Brooklyn, New York 11232 Phone: (718) 965-5301	New York (Southern Portion)
Orlando 7200 Lake Ellen Drive Suite 120 P.O. Box 118 Orlando, Florida 32802 Phone: (407) 855-0900	Florida
Philadelphia 900 U.S. Courthouse 2nd and Chestnut Streets Philadelphia, Pennsylvania 19106 Phone: (215) 597-4393	Delaware, Pennsylvania
San Francisco Federal Office Building Room 506 U.N. Plaza San Francisco, California 94102 Phone: (415) 556-6163	California (Northern), Hawaii, Nevada

District	State Served
San Juan Fernandez Juncos Avenue Stop 8½ Puerta de Tierra San Juan, Puerto Rico Phone: (809) 729-6842	Puerto Rico (MAIL to: P.O. Box 5719 Puerta de Tierra Station San Juan, Puerto Rico 00906)
Seattle 22201 23rd Drive, S.E. Bothell, Washington 98021 Phone: (206) 486-8788	Alaska, Idaho, Oregon, Washington (MAIL to: P.O. Box 3012 Bothell, Washington 98041)

APPENDIX C
List of Acronyms

CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CFR	Code of Federal Regulations
DHHS	Department of Health and Human Services
DSMA	Division of Small Manufacturers Assistance
EIR	Establishment Inspection Report
FDA	Food and Drug Administration
FD&C	Food, Drug, and Cosmetic
FOI	Freedom of Information
FR	Federal Register
GMP	Good Manufacturing Practices
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
NDA	New Drug Application
OTA	Office of Training and Assistance
PDP	Product Development Protocol
PMA	Premarket Approval Application

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